Clinical Reports

Bronchogenic Adenocarcinoma in a Hyacinth Macaw (Anodorhynchus hyacinthinus)

Wes A. Baumgartner, DVM, David Sanchez-Migallon Guzman, Lcdo en Vet, Shawn Hollibush, DVM, Lorrie Gaschen, PhD, Dr habil, DVM, Dr Vet Med, Dipl ECVDI, E. Clay Hodgin, DVM, PhD, Dipl ACVP, and Mark A. Mitchell, DVM, MS, PhD

Abstract: An adult female hyacinth macaw (*Anodorhynchus hyacinthinus*) was presented for sudden onset of severe weakness in the legs. Neurologic examination revealed bilateral paresis of the pelvic limbs and decreased proprioception. Results of radiographs and computed tomography (CT) revealed variably sized soft tissue nodules throughout the lungs and invading into the spine and vertebral canal. Soon after the CT scan, the bird went into cardiorespiratory arrest and died. At necropsy, several yellow, coalescing nodules that were firm with a caseous component were present in the lungs, and a focus of similar tissue was attached to the vertebrae and invaded the spinal canal. On histologic examination, the diagnosis was primary pulmonary bronchial adenocarcinoma with spinal invasion.

Key words: bronchogenic pulmonary adenocarcinoma, pathology, psittacine, avian, hyacinth macaw, *Anodorhynchus hyacinthinus*

Clinical Report

A 1.25-kg adult female hyacinth macaw (*Ano-dorhynchus hyacinthinus*) of unknown age was presented for sudden onset of leg weakness. The bird had no clinical signs of disease when the owners had left for the weekend, but upon returning, the bird was found at the bottom of the enclosure unable to perch or ambulate. This bird was housed with a male hyacinth macaw in an outdoor enclosure at the owner's aviary. In total, the owners had 11 birds at the facility. The diet consisted of commercial formulated pellets supplemented with nuts, fruit, and monkey chow.

On physical examination, the bird was alert and responsive but in sternal recumbency, was mildly dehydrated (as indicated by loss of eyelid turgor and delay in basilic vein refill time), and had a body condition score of 2/5.¹ Overall feather quality was poor and the skin was mildly bruised with abrasions present over the dorsum of the bird and bilaterally on the radiocarpal joints. Neurologic examination revealed paraparesis as well as impaired proprioception (evaluation of the knuckling of toes while supporting the bird) of both legs. Deep pain perception appeared still present because the bird visibly reacted to stimuli. The primary differential diagnoses for the paraparesis were spinal subluxation or fracture, nutritional disease, infectious disease, vascular accident, hepatic or renal disease, neoplasia, and heavy metal toxicosis.

Results of a complete blood cell count revealed moderate leukopenia (4900 cells/µl; reference range, 6000–12 000 cells/µl). Results of a plasma biochemical analysis revealed moderate increases in concentrations of creatine kinase (5908 U/L; reference range, 100–300 U/L) and uric acid (27 mg/dl; reference range, 2.5–11 mg/dl) and a mild decrease in albumin concentration (1.2 g/dl; reference range, 1.2–3.1 g/dl) and in the albumin to globulin ratio (0.75; reference range, 1.6–4.3).² Blood levels of zinc, lead, and copper were within

From the Department of Pathobiological Sciences (Baumgartner, Hodgin) and the Department of Veterinary Clinical Sciences (Guzman, Hollibush, Gaschen, Mitchell), Louisiana State University School of Veterinary Medicine, Skip Bertman Dr, Baton Rouge, LA 70803, USA. Present address: University of Illinois, College of Veterinary Medicine, Department of Veterinary Clinical Medicine, 1008 W Hazelwood Dr, Urbana, IL 61802, USA (Mitchell); Stillwater Veterinary Clinic, 2020 Curve Crest Blvd, W Stillwater, MN 55082, USA (Hollibush).



Figure 1. Lateral radiograph of a hyacinth macaw that presented for acute onset of weakness of the legs. A diffuse and poorly marginated soft tissue opacity is superimposed with the cranial thoracic vertebrae. The margins of the vertebrae are poorly discernible especially at their ventral margins (black arrows).

reference ranges. Results of aerobic bacterial culture of a cloacal swab sample revealed a mixed culture, including alpha- and gamma-hemolytic *Streptococcus* species as well as *Escherichia coli*.

Lateral and ventrodorsal digital radiographs of the body were performed. Results showed a diffuse and poorly marginated soft tissue opacity superimposed with the cranial thoracic vertebrae just caudal to the scapula (Fig 1). The margins of the vertebrae were poorly discernible in this region. In the ventrodorsal view (Fig 2), a poorly marginated soft tissue opacity was present in the cranial aspect of the left lung. The caudal border of the opacity had a somewhat rounded and more defined margin. Differential diagnoses for the left-sided pulmonary lesion were fungal pneumonia such as aspergillosis, bacterial pneumonia, and neoplasia. Complete assessment of the thoracic spine was not possible because of the superimposed soft tissues of the lung. A computed tomography (CT) examination of the spine was recommended because of the macaw's clinical signs.

Initial therapy consisted of balanced crystalloid fluids given by intravenous bolus (15 ml/kg) and subcutaneously (100 ml/kg q12h). Calcium- EDTA (35 mg/kg SC q24h), dexamethasone sodium phosphate (4 mg/kg IM once), pipercillin/tazobactam (125 mg/kg IM q12h; Zosyn, Wyeth Pharmaceuticals, Philadelphia, PA, USA), and metronidazole (50 mg/kg PO q24h) were also administered. Treatment with calcium-EDTA was discontinued after the results of the blood zinc, lead, and copper analysis were reported as normal.

Three days after initial presentation, the bird continued to have a good appetite and normal

fecal output. Subsequent neurologic examinations revealed no changes. Abnormalities on repeat hematologic and biochemical testing at this time were leukopenia (3700 cells/µl), a mild increase in glucose concentration (365 mg/dl; reference range, 145–345 mg/dl),² a marked increase in creatine kinase concentration (24 310 U/L), and a continued moderate increase in uric acid concentration (26 U/L). Albumin concentration and albumin : globulin ratio remained unchanged. A regimen of allopurinol (10 mg/kg PO q12h) was initiated to control the hyperuricemia.

A CT was performed to better assess the nature of the paresis and pulmonary opacities. The bird was induced with isofluorane (5%, 1 L O₂/min) by mask, intubated with 4.0-uncuffed endotracheal tube, and maintained under general anesthesia (2%, 1 L O₂/min) for the procedure.

The CT examination was performed with 1-mm slices through the entire thoracic and sacral spinal column. Variably-sized, well-marginated, soft tissue dense nodules were present throughout the lungs. In the cranial aspect of the left lung, a diffuse, soft tissue dense region was adjacent to the thoracic vertebrae (Fig 3). At this site, the ventral margin of the left transverse process was disrupted, and the trabecular bone contained multifocal lucencies. Invasion of the spinal canal was suspected on subsequent slices, but because of the limits of resolution, this was difficult to confirm. Because of the presence of an aggressive bone lesion and pulmonary nodules, neoplasia was considered the most likely diagnosis. Within a few hours after an uneventful recovery from anesthe-



Figure 2. Ventrodorsal radiograph of the hyacinth macaw described in Figure 1. A poorly marginated zone of increased opacity is present in the left cranial thorax. The caudal border of this lesion is rounded and better defined than at its cranial aspect (black arrows).

sia, the macaw developed increased respiratory effort and harsh lungs sounds, which progressed rapidly to cardiorespiratory arrest. Initial resuscitation efforts were successful, but the patient arrested again and was unable to be revived.

At necropsy, the left lung contained several 5– 10-mm-diameter pale yellow, coalescing nodules that were firm and had a large caseous component. The left side of the anterior thoracic spine (notarium) had a focus of irregular, pale yellow, slightly firm tissue intimately attached to the vertebral body between the transverse and ventral spinous processes. This focus was 1 cm long and 5 mm wide and invaded the spinal canal (Fig 4). The infiltrating tissue compressed the spinal cord,



Figure 3. High-resolution transverse computed tomography image of the thorax of the hyacinth macaw described in Figure 1. Slice thickness is 1 mm. Multiple, variably-sized, homogeneous, soft tissue dense nodules are visible throughout the lung parenchyma (white arrows). A soft tissue dense structure is adjacent to the thoracic vertebral body and the transverse process is disrupted (black arrows). Multifocal lucent areas are present within the trabecular bone in the same region.

extended caudally along the spinal canal for 1.5 cm, and effaced bone. Also present were several 1- to 2-mm-wide dorsoventrally flattened, rounded, firm, dull yellow nodules that slightly bulged into the wall of the aorta and the proximal brachiocephalic arteries. Sections of formalin-



Figure 4. Gross transverse sections of the thoracic spinal column of the hyacinth macaw described in Figure 1. The spinal cord is visible (large white arrows). A mass (small arrows) is visible infiltrating the spinal canal and effacing vertebral bone. Top of the photo corresponds to the dorsum.



Figure 5. Photomicrograph of the lung tumor from the hyacinth macaw described in Figure 1. The tumor is composed of a dense cellular component admixed with fibrous tissue that effaces normal lung stroma. Parabronchi are visible (black arrows) (hematoxylin and eosin, $\times 40$).

fixed tissues were submitted for histopathologic examination.

Microscopically, the pulmonary nodules were well demarcated but unencapsulated and infiltrative. Densely cellular neoplastic masses primarily involved secondary bronchi, parabronchi, and, less commonly, mesobronchi (intrapulmonary primary bronchi) (Fig 5). Neoplastic cells were continuous with normal bronchial epithelium. Tumors were composed of tubuloacinar structures and cords surrounded by desmoplastic stroma. Multifocally within the atria of the parabronchi, cells formed polypoid to cribiform to polyadenoid structures that often bridged



Figure 6. Higher magnification of the tumor in Figure 5. Cells are arranged in tubuloacinar and cribiform structures that bridge interatrial septa (hematoxylin and eosin, $\times 200$).



Figure 7. Photomicrograph of the lung tumor described in Figure 5. The wall of a bronchus (arrow designates a bronchial cartilaginous plate) is expanded and effaced by a densely cellular and fibrous mass (hematoxylin and eosin, $\times 100$).

interatrial septa (Fig 6). Large acinar structures were lined by pseudostratified ciliated columnar epithelium interspersed with mucosecretory cells, whereas small acini and polypoid structures were lined by simple, cuboidal to attenuated epithelium with rare goblet cells. Acinar structures were filled with periodic acid–Schiff–positive, basophilic mucus and lesser amounts of hemorrhage, various degenerate cells, and macrophages. Neoplastic tissues invaded the walls and entered the lumina of a primary bronchus and large vein (Fig 7). Within the center of a nodule were multiple large, irregular, partially mineralized structures that resembled fibrocartilaginous plates. Neoplastic



Figure 8. Photomicrograph of the center of a lung nodule from the macaw described in Figure 1. Multiple, partially mineralized fibrocartilaginous plates can be seen in contact with large acinar structures (hematoxylin and eosin, $\times 100$).



Figure 9. Photomicrograph of the spinal column (sagittal section) as shown in Figure 4. The top of the image corresponds to the dorsum of the macaw. Widespread axonal degeneration can be seen as generalized pallor in the spinal cord. An area of spinal cord associated with an intervertebral joint is compressed (small arrow). The mass (large black arrow) fills the spinal canal and compresses the spinal cord (hematoxylin and eosin, $\times 20$).

epithelial cells were in intimate contact with these plates, and in some areas, cells were trapped within the matrix (Fig 8). Focally, a large section of a neoplastic nodule was infarcted.

On histologic examination of the spine, similar neoplastic tissues filled the vertebral canal. Multifocally, the mass destroyed vertebral trabeculae and expanded into the associated vertebral air spaces. The spinal cord at this level was compressed by the mass and exhibited marked axonal degeneration with spheroids and widespread compression necrosis (Fig 9). The nodules present in the great vessels were characteristic of atheromatous change, characterized by thickening of the tunica media by foamy cell infiltration admixed with clear acicular structures (cholesterol) and an amorphous ground substance that was occasionally mineralized. On the basis of the epithelial morphology, continuity with airways, and predominance within pulmonary tissues, bronchogenic adenocarcinoma was diagnosed. Cerebrum, liver, heart, intestine, thyroid, spleen, kidney, ventriculus, pancreas, and proventriculus were grossly and microscopically within normal limits.

Discussion

As with domesticated mammals, primary lower respiratory tract neoplasms in pet birds are infrequent to rare, and detailed reports are few.³⁻⁹ Primary lung carcinomas have been described in an African grey parrot (Psittacus erithacus) and a Moluccan cockatoo (Cacatua moluccensis) experiencing musculoskeletal signs and paraparesis, respectively.^{3,4} A primary air sac carcinoma and an axillary cystadenocarcinoma of undetermined origin have also been reported in 2 Moluccan cockatoos.^{5,10} The outcome was grave in 3 of the 4 cases.^{3–5,10} In this report, we document the clinical and pathologic findings in a hyacinth macaw with a bronchogenic adenocarcinoma that presented for paraparesis. Reports of neoplasms in hyacinth macaws are rare but include hepatic adenocarcinoma, splenic erythroblastosis, myelolipoma, and cloacal papilloma.11-13

In 2 surveys of neoplasia spanning multiple avian orders, the incidence of pulmonary neoplasia ranged from 0.1% to 0.2% of all cases submitted.14,15 Of all neoplasms diagnosed in the most recent of these surveys (exclusively avian), only 20 of 557 (3.6%) were of respiratory origin, all were malignant, and most were considered to be the cause of death.¹⁴ A second survey involving more than 19 000 necropsies (including mammals) from the Philadelphia Zoo found only 20 cases of avian pulmonary neoplasia, 18 of which were malignant.15 Most of these cases involved ducks or waterfowl and, on the basis of other published reports, ducks might be more prone than other species to primary pulmonary tumors.^{9,15} Pulmonary neoplasia in poultry, likewise, is rare when virally induced neoplasms are excluded.9 Furthermore, a survey of 1539 cases of neoplasia in pet birds found only 7 respiratory tumors, 5 of which were in the lungs.¹³

Detailed accounts of primary lower respiratory neoplasms in pet birds, whether from the lung or air sac, have been reported rarely.⁶ In large psittacine birds, of 4 such cases found, only 2 were considered to originate from the lungs.^{3,4} An African grey parrot diagnosed with bronchial carcinoma with metastasis to the right humerus presented with right wing drooping, shoulder and elbow ankylosis, and poor body condition. The mass described in that case shared many microscopic features with this case, including continuity between bronchial and neoplastic epithelium, ciliated epithelium, polyadenoid morphology, vascular invasion, and bone destruction.³ The second case concerned a Moluccan cockatoo with paraparesis because of a highly cellular lung mass that primarily invaded the vertebral column and right humerus.⁴ Like the present case, this mass infiltrated the spine overlying the lungs. The microscopic nature of this mass, however, was very different than that of reports discussed here, including the present case, in that this mass formed sheets of pleomorphic and multinucleate cells.

The remaining 2 reports involve Moluccan cockatoos with grossly evident masses in the right axillary region.^{5,10} In one of these, a multicystic mass with significant serosanguineous drainage was diagnosed as an axillary cystadenocarcinoma of respiratory origin.¹⁰ As in the present case, it was composed of acini, cysts, and tubulopapillary structures in mild to moderate stroma. Multiple small neoplastic foci were also present throughout the lungs and were seen to invade the humerus. Interestingly, reovirus-like particles and inclusions were found in neoplastic cells but were considered incidental. The second case report described a mucinous adenocarcinoma originating from the air sac of the right humerus.⁵ This neoplasm was populated by pseudostratified columnar epithelium that formed glands, similar to the present case. But unlike other cases mentioned, mucinous cells and myxomatous stroma formed a large portion of this mass. Furthermore, like the present case, cartilaginous and osseous tissues were present within the mass, although in much larger quantities. Osseous and cartilaginous pulmonary foci are known to form in commercial poultry because of pulmonary congestion and edema.¹⁶ In the present case, the focal region of chondro-osseous tissue might have been simply osseous metaplasia in bronchial cartilage, which is known to occur in certain human lung neoplasms.¹⁷

In the case we describe, no respiratory signs were observed on presentation, however paraparesis was present and this was directly attributable to the neoplastic compression of the spinal cord by the mass. Differential diagnoses for sudden onset of paraparesis in birds include, but are not limited to, metabolic (renal, endocrine) and nutritional (thiamine, vitamin E deficiency) abnormalities, neoplasia (gonadal, hepatic, renal, intestinal, musculoskeletal, pulmonary, and nervous system), infectious disease (*Chlamydophila psittaci*, *Mycobacterium avium*, paramyxovirus, herpesvirus, retrovirus, *Aspergillus* species, *Toxoplasma gondii*, other), inflammatory disease (polyneuropathy), toxicoses (heavy metals, organophosphates, carbamates, and chlorinated hydrocarbons), traumatic insult, and vascular disease (thromboembolic disease).^{18–22} Hyperuricemia is seen in cases of renal disease, severe dehydration, tissue damage, starvation, and other various causes.²³ In this case, because renal disease and severe dehydration were ruled out, ongoing tissue damage caused by sternal recumbency was the likely cause.

The diagnosis in most cases is made late in the course of the disease or on postmortem examination. In our case, results of initial blood work indicated possible prerenal or renal involvement and soft tissue damage. Radiographs and CT enabled us to identify the location and extension of the lesion. In birds, the differential diagnoses for increased soft tissue opacities in the lungs are infectious granulomas (bacterial, Aspergillus species, other), aspiration pneumonia, and neoplasia. Fine-needle aspiration and biopsy of the pulmonary masses would have been the next step toward an antemortem diagnosis. Biopsy samples of the avian lung can be collected by laparoscopy through the caudal thoracic air sac or via coelioscopy.²⁴ Other diagnostic tests considered were magnetic resonance imaging (MRI), nuclear scintigraphy, myelography, and cerebrospinal fluid analysis. To examine the lung and bony structures of the spine, CT is preferred over MRI. In this macaw, MRI would not have allowed the detailed examination of the lung. Spinal canal invasion and examination of the nervous tissues is certainly an advantage of MRI over CT, however. Also, MRI appears to be more accurate than CT in the diagnosis of mediastinal invasion.25 Nuclear scintigraphy has also been proven successful in identifying spinal abnormalities in birds.²⁶ In our case, it might have provided additional information regarding the presence of occult metastases. Myelography has been used rarely in avian species, but a myelographic technique for avian species has been described in chickens by entry through the thoracolumbar region.²⁷ Although myelography could have been attempted together with CT for contrast enhancement, it was deemed unnecessary because of the evident nature of the lesions. Analysis of a cerebrospinal fluid sample can be used alone or in conjunction with myelography to characterize infectious, neoplastic, and inflammatory disorders of the spinal cord or brain. Access to the subarachnoid space or fourth ventricle can be achieved, but the risk of the cisternal puncture in small birds is high. $^{\rm 28}$

There are no reports regarding treatment and prognosis of pulmonary neoplasms in birds except in the case of the Moluccan cockatoo with the axillary mucinous adenocarcinoma. In that case, the presence of the mass in the wing allowed surgical resection. In dogs and cats, most primary lung neoplasms are best treated by surgical excision.29 Chemotherapy has been largely unreported, but in a very limited series of cases, multidrug chemotherapy regimens have shown some benefit.²⁹ Radiation therapy is rarely used in small animals as adjunctive treatment of pulmonary neoplasms. In humans affected by metastatic spinal lesions from pulmonary neoplasms, treatment includes chemotherapy, radiotherapy protocols, and, in some cases, surgery to decompress the spinal cord. In cases of vertebral metastasis, the mean survival time in humans with lung cancer after diagnosis was 7.1 months.³⁰ In our case, the invasiveness and extent of lung tissue affected would have made supportive therapy the optimal treatment.

In most cases of primary lower respiratory tract neoplasia in psittacine birds, antemortem diagnosis is difficult and often done at a late stage of disease. Presentation usually involves the presence of an obvious mass or signs related to bone invasion, the latter of which was seen in all cases discussed above. Interestingly, the right humerus was invaded by neoplasia in all 4 previous reports and 3 of the 4 involved Moluccan cockatoos.

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